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# THE EFFECT OF ESTROGENIC ACTIVITY OF KANJIBHAVIT JAPAKUSUMA ON THE ENDOMETRIUM OF WISTER ALBINO RATS

Ayurveda

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## ABSTRACT

Estrogens are female sex hormones, and they play an essential role in the development of female secondary sexual characters and regulate the menstrual cycle and reproductive system. Estrogen is considered the dominant hormone of the proliferative phase and induces mucosal proliferation during the proliferative phase1. Estrogen increases the mitosis rates of both glands and stroma, an effect that stimulates the growth and thickening of the endometrium2. Hence, the present study has been planned to assure the evaluation of the estrogenic activity of Kanji Bhavit Japakusuama, an oral formulation, in Wister Albino rats. The test formulation was administered to animals for 21 consecutive days. Histology parameters of the uterus are carried out. The estrogenic activity of Kanji bhavit japakusuma was found to be responsible for playing a significant role in stimulating the growth and maturation of the endometrium of the uterus in Wister albino rats.

## KEYWORDS

Kanjibhavit Japakusuma, Estrogenic Activity.

## INTRODUCTION

Endometrium is the primary target tissue for estrogen. There is improved vascularity with hyperplasia of the muscles of the uterus. Cyclic changes in the endometrium comprise regeneration and proliferation of the endometrium.

Oestrogen also produces receptors for progesterone, which cause withdrawal of oestrogen and lead to the shedding of endometrium. Oestrogen causes proliferation of endometrial glands, growth and compaction of stroma.[3]

The events are highly complex and include repair of the endometrium surface, proliferation, angiogenesis, vasculogenesis, cell differentiation and extracellular matrix remodeling.[4]

Oestrogens restore the endometrium, including the arteries, after menstruation. Estrogen induces mucosal proliferation during the proliferative phase and progesterone receptor synthesis.[5]

## MATERIAL AND METHODS

### Drug Sample

- *Kanjibhavit japakuausma* consist of *japakusuma* flower , *purana guda* and *kanji.*
- 70g of *japakusuma* flower was added with equal amount of *purana guda* and made into *kalka* form. 20 ml *kanji* was taken to which 400 mg of above *kalka dravya* was added and *bhavana* was done.
- Dose was fixed according to the body weight and was administered orally. *Kanji bhavit japakusuma kalka* taken as test drug to be given internally.

### Animals

Wistar strain albino female rats weighing between 150-250g were used for experimental study with following conditions. The animals were obtained from the animal house attached to the pharmacology laboratory, SDM centre for research in ayurveda and allied science. Udyavara.

They were exposed to natural day and night cycles with ideal laboratory condition in terms of ambient temperature, humidity. They were fed with saidurga feeds, bengalooru rat pellets and tap water ad libitum. The experiments would be carried out in conformity with guidelines of the institutional animal ethical committee (IAEC) after obtaining its permission. Ethical CLEARENCE NO. SDMCRA/ IAEC/UD-PT-16 ON 29/5/2017.

**Animal grouping**: the selected animal grouped into five groups with 6 animals each. Group A, only water and normal diet administered . Whereas group B ovariectomized control group only water and normal diet administered and served as positive control group.

In group C ovariectomized animals treated with kanji bhavita japakusuma at therapeutic dose. In group E normal rats treated with *kanji bhavita japakusuma* at therapeutic dose. The group D ovariectomized animals treated with standard drug.

### Animal Grouping

| Group | No. Of rats | Drugs |
|---|---|---|
| A | 6 | Normal control |
| B | 6 | Positive control ( oophorectomized) |
| C | 6 | Test drug + (oophorectomized) |
| D | 6 | Standard drug (Norethisterone ) |
| E | 6 | Test drug |

Dose calculation: the dose determination of test drug will be carried out based on acute oral toxicity report AOT will be carried out following OECD GUIDELINES 425.

**Test Drug**: *kanji bhavit japakusuma kalka* taken as test drug to be given internally.

- Acute oral toxicity study
- The test drug *kanjibhavit japakusuma* was screened for acute toxicity to OECD425 GUIDELINES.

### Drug Administration

Direct administration of the drug was done without any vehicle as the formulation was liquid . Drugs were administrated by oral route by the help of feeding tube with injection syringe and duration for 21 days

### OBSERVATION PARAMETERS

**(I) Histopathology :** Uterus

## RESULT

### Overiectomised Control Group

| Rat no and section | Changes observed | Remarks |
|---|---|---|
| 1 | Glandular damage and atrophy. Endometrial atrophy. Increased Neutrophils in endometrium. Loosely arranged stromal tissue with decreased blood vessels. | Moderate degenerative changes and inflammation |
| 2 | Atrophied endometrium. Damaged and decreased number of glands. Stroma loosely arranged. Decreased blood vessels. | Severe degenerative changes |
| 3 | Hyperplastic epithelium. Hyperplastic glands. Dilated lumen of endometrium in glands. Damaged glandular architecture. Abundance of eosinophils. | Severe degenerative changes with acute inflammation |
| 4 | Apoptotic changes of cells in epithelium and glands. Glandular architecture damaged. Dilated lumen of endometrium | Moderate degenerative changes |
| 6 | Hyperplastic epithelium. Hyperplastic glands. Dilated lumen of endometrium in glands. Damaged glandular architecture | Severe degenerative changes |

| | | |
|---|---|---|
| Extra | Vacuolated cells in glands. Abundance of eosinophils. | Mild degenerative changes with inflammation. |

**Test Drug Overiectomised Group**

| Rat no and section | Changes observed | Remarks |
|---|---|---|
| 1 | Only few cells of epithelium showed apoptosis. Slight glandular damage. Stroma loosely arranged. Muscular layer slightly disorganized | Mild degenerative changes |
| 2 | Atrophy of endometrium. Severe proliferation of stroma. Hypercellular. Decreased number of glands | Mild degenerative changes. Proliferative activity |
| 3 | Atrophied epithelium. Severe cellular and stromal proliferation. Increased number of glands | Mild degenerative changes. Proliferative activity |
| 4 | Atrophied epithelium. Severe cellular and stromal proliferation. Glandular damage seen | Mild degenerative changes Proliferative activity |
| 5 | Hyperplasia of epithelium. Abundance of neutrophils. Glandular architecture almost normal. Increase in blood vessels. | No degenerative activity. Inflammation seen |
| 6 | Decreased glands. Severe stromal proliferation and hypercellular layers. | Proliferative activity |
| 7 | Epithelial hyperplasia. Stroma fibrosed in some areas. Proliferation of stroma and hypercellular layers. Gland damage seen | Mild degenerative activity with proliferation |
| Extra | Decreased glands. Severe stromal proliferation and hypercellular layers. | Proliferative activity |

**Standard Group**

| Rat no and section | Changes observed | Remarks |
|---|---|---|
| 1 | Endometrial atrophy. Hyperplasia of glands. Some glands damaged. Proliferation of stroma and hypercellular layers. | Moderate degenerative changes |
| 2 | Epithelium cuboidal. Glands dilated and less in number. Cystic change of glands. Stroma hyalinized. Proliferation of stroma and hypercellular layers. More blood vessels. | Moderate degenerative changes. Proliferative activity. |
| 3 | Epithelium cuboidal in some areas. Glands almost normal. Proliferation of stroma and hypercellular layers. | No degenerative changes. Proliferative activity. |
| 4 | Epithelium atrophic. . Proliferation of stroma and hypercellular layers. Gland damage seen in some areas. | Mild degenerative changes. Proliferative activity |
| 5 | Epithelium atrophic. . Proliferation of stroma and hypercellular layers. Gland damage and hyperplasia seen in some areas | Mild degenerative changes. Proliferative activity |
| Extra | Epithelium atrophic. Proliferation of stroma and hypercellular layers. Gland damage seen in some areas. | Mild degenerative changes. Proliferative activity |

**Test Drug**

| Rat no and section | Changes observed | Remarks |
|---|---|---|
| 1 | Epithelium atrophic. Proliferation of stroma and hypercellular layers. Glandular architecture almost normal | Mild degenerative changes. Proliferative activity |
| 2 | Epithelium atrophic. Proliferation of stroma and hypercellular layers. Dilated lumen and glands | Mild degenerative changes. Proliferative activity |
| 3 | Epithelium atrophic in 1 area. Proliferation of stroma and hyper cellular layers. Few glands show normal architecture | Mild degenerative changes. proliferative activity |

## DISCUSSION

The role of phytoestrogens which are present in kanji bhavit *japakuauma* ,like flavonoids exert their effect primarily binding to the estrogen receptor and reported for their estrogenic activity [6].

In Overitomised control group, the sections showed damage in glands. The stroma is loosely arranged. The sections showed moderate to severe degenerative activity.

In Test drug Ovariectomised Group, The glandular damage is reduced compared to overiectomised control group. Severe proliferation of stroma, cells of muscular layer are seen. The sections showed mild degenerative activity with proliferative activity.

In standard group, showed severe proliferation of stroma and hypercellular muscular layer. Glandular damage seen to some extent. Damage is less compared to overiectomised control.

In test drug ,showed severe proliferation of stroma and hypercellular muscular layer. Epithelial and Glandular damage was less compared to overiectomised control group.

## CONCLUSION

The Kanji bhavit japakusuma formulation may play a significant role in the proliferation and thickening of endomaterium[7] by estrogenic activity. Estrogen has been shown to stimulate endometrial cell proliferation.[8,9]

In the present experimental study of kanjibhavit japakusuma showed less damage and increased growth and proliferation of endometrium of uterus with the help of estrogenic activity.[10,11] The kanji bhavit *Japakusuma* can be used as an herbal drug for estrogenic activity, which is needed for further improvement of several parameters.

**Histopatology – Uterus**

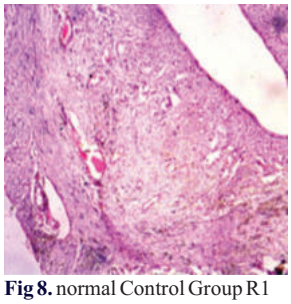

**Fig 8.** normal Control Group R1

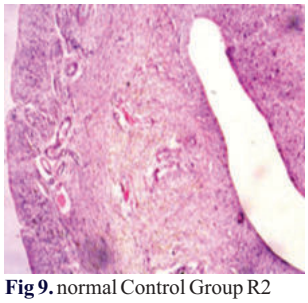

**Fig 9.** normal Control Group R2

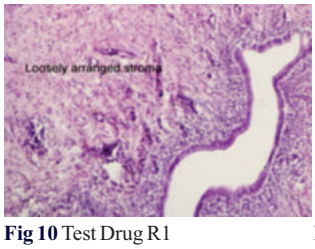


**Fig 10** Test Drug R1

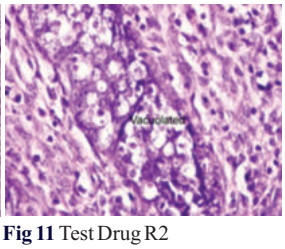


**Fig 11** Test Drug R2

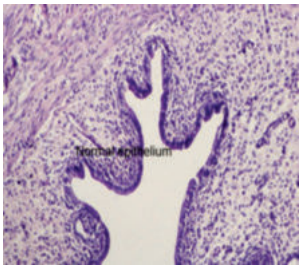


**Fig 12** Positive Control (o) R1

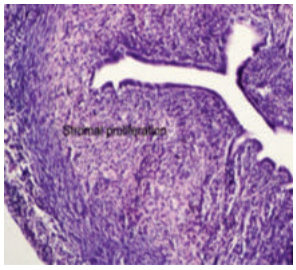


**Fig. 13** Positive Control (o) R2

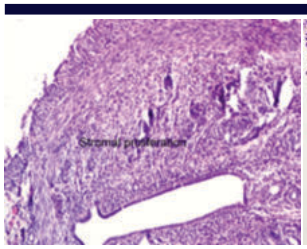


**Fig .14** Test Drug (o) R1

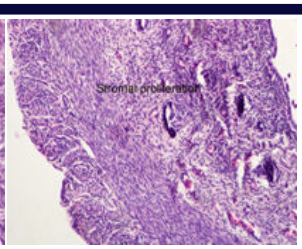


**Fig .15** Test Drug (o) R2

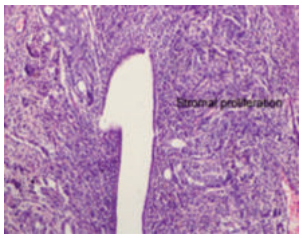


**Fig .16** Standard Drug (o) R1

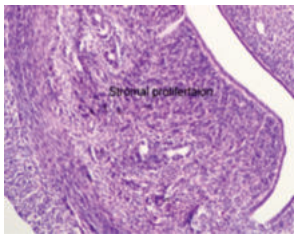


**Fig .17** Standard Drug (o) R2

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